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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,175	02/24/2006	Thomas Schnelle	46955.21	8784

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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

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05/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,175	SCHNELLE ET AL.	
	Examiner	Art Unit	
	ROBERT KASTEN	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first non-final action on the merits.

Claims 2-29 are pending in this application. Claim 1 has been cancelled.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear in light of the specification what structural limitations "different structured edges" encompasses. The examiner has construed it to mean that the **edges** are **shaped differently**, or in other words that they are differing angles or directions (i.e. shapes).

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 29, 2, 4-12, 14-15, 17, 19, 25 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by GAWAD et. al. (EP 02 002 437.8), from here on referred to as GAWAD. For convenience, the publication US 2003/0178310, which claims priority to EP 02 002 437.8, is used as an English language equivalent.

Concerning the independent claim 29, GAWAD teaches a claim 16, whose limitations are directed to a method for sorting particles comprising the following steps:

a) flowing particles in a fluid flow

b) positioning the particles in the physical center of the fluid flow (analogous to "predetermined space relative to the impedance detector) using dielectrophoresis

c) characterizing the separated particles by using an impedance measurement.

Concerning Claim 2, GAWAD teaches all the limitations of claim 29. Further, GAWAD teaches the focusing of the particles to the center of the fluid flow takes place upstream of the impedance detector, since the particles are first focused to the center of the flow channel and then pass into the measuring channel (both [0013] and [0016]).

Concerning Claim 4, GAWAD teaches all the limitations of claim 29. Further, GAWAD teaches that the measuring electrodes are arranged on the walls of the microchannel [0018]. Since the particles are dielectrophoretically focused to the center of the microchannel [0015], the particle inherently moves in a part of the fluid whose perpendicular projection is onto the wall of the microchannel. Finally, since the

microchannel is the same for focusing and measuring, the impedance detector is arranged on this same wall.

Concerning Claim 5, GAWAD teaches all the limitations of Claim 29. Further, GAWAD teaches that the focusing of the particles occurs by funneling the particles to the center of the flow channel [0015]. Since the measuring electrodes are arranged on the walls of the flow channel, it is inherent that any particles on the opposite sides of the flow channel from the measuring electrodes will be funneled into a flow path closer to the measuring electrode. Further, GAWAD teaches the use of a deflection electrode (electrode 26 from figure 5b) described in [0052] in one embodiment of the measuring portion of the invention, which dielectrophoretically deflects the particles towards one measuring electrode (electrode 24 from figure 5b.)

Concerning Claim 6, GAWAD teaches all the limitations of claim 29. Further, GAWAD teaches that the particles to be focused and measured are biological cells [0040].

Concerning Claim 7, GAWAD teaches all the limitations of claim 29. Further, GAWAD inherently teaches that the impedance value is evaluated in relation to the characteristics of the particles. In [0022], GAWAD teaches that the particles may be sorted based on upstream impedance measurements according to their cell membrane characteristics as well as the presence and/or activity of cell membrane receptors. The membrane characteristics and receptors of a cell provide the cell with its dielectric characteristics and are inherently linked to their measured impedance [0016]. Therefore, if GAWAD's invention is able to sort cells according to these parameters, the

invention must be able to measure and determine the impedance based on these parameters.

Concerning Claim 8, GAWAD teaches all the limitations of claim 29. Further, GAWAD teaches that the invention permits the measurement of not only impedance, but also the velocity and position of the cells [0022]. This information is needed to help with downstream sorting of the cells, and therefore inherently must be used to help establish a time component so that the sorting may be effective.

Concerning Claim 9, GAWAD teaches all the limitations of claim 8. Further, GAWAD teaches that the invention permits the measurement of not only impedance, but also the velocity and position of the cells [0022]. Additionally, GAWAD teaches that the flow channel has a cross-section only slightly larger than that of the cell [0016]. Inherently, the flow speed of the fluid will be identical to the flow speed of the cell in this case.

Concerning Claim 10 and 11, GAWAD teaches all the limitations of claim 8. Further, GAWAD teaches that passage of a cell through the measurement channel (which contains the measurement electrodes [0050]) is measured with respect to changes in electrical impedance [0016]. The shapes of the electrodes are not limiting to the claimed method.

Concerning Claim 12, GAWAD teaches all the limitations of claim 8. Further, GAWAD teaches the use of two sets of electrodes in the measurement channel which correspond to two different impedance detectors [0050].

Concerning Claim 14, GAWAD teaches a device for focusing cells and measuring the impedance of a channel which is best exemplified by figures 3a and 5a. Specifically, the device comprises the following features:

a) an impedance detector in a microchannel containing a fluid (24 or 25 in figure 5a).

b) a focusing device with oblique electrodes which form a funnel in the microchannel for dielectrophoretically focusing a particle to the center of the channel (electrodes 20 and 21 with particle 17 in figure 3a). These electrodes produce a funnel shaped field barrier [0044].

Concerning Claim 15, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches the focusing of the particles occurs upstream from the measurement channel [0015].

Concerning Claim 17, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches the focusing electrodes may be in an arrangement of two consecutive electrodes which are arranged obliquely to the walls of the microchannel and act to funnel cells and cell clusters into a stream of single cells at the center of the flow channel ([0049] and figure 4).

Concerning Claim 19 and 27, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches a plurality (2) of detecting electrodes in the measurement channel, each one disposed on the wall of the channel (features 24 and 25 from figure 5a).

Concerning Claim 25, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches in a figure 5a, which shows two impedance detector electrodes (24, 25) which are arranged on the upper and lower walls of the microchannel and which extend across the micrcohannel, perpendicular to the fluid flow.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 3, 13, 16, 18 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over GAWAD.

Concerning Claim 3, GAWAD teaches all the limitations of claim 29. Further, GAWAD teaches the focusing of the particles to the center of the fluid flow takes place upstream of the impedance detector, since the particles are first focused to the center of the flow channel and then pass into the measuring channel (both [0013] and [0016]). According to MPEP 2144.04 VI, C, a rearrangement of parts (such as moving the focusing from upstream of the detector to on the detector) does not necessarily yield an unobvious invention. By example, "the particular placement of a contact in a conductivity measuring device was held to be an obvious matter of design choice (In re Kuhle, 526 F.2d 553, 188 USPQ7 (CCPA 1975)." One of ordinary skill in the art would have known that moving the focusing step on to the detecting step would have yielded a simpler device, eliminating the need for extraneous microchannels between focusing and detection and possibly allowing for simpler electrode setups.

Concerning Claim 13, GAWAD teaches all the limitations of claim 29. GAWAD also teaches that the impedance measurements are taken at a plurality of frequencies [0051]. Further, GAWAD teaches that dielectrophoresis occurs at frequencies between 100 kHz and 10 MHz depending on the liquid and particles. It would have been *prima facie* obvious to one of ordinary skill in the art to also focus the cells at different frequencies using the device of GAWAD because doing so would allow the device to

focus multiple cell types, which would be obviously advantageous in a device ultimately used to sort cells according to like characteristics like membrane composition.

Concerning Claim 16, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches the focusing of the particles to the center of the fluid flow takes place upstream of the impedance detector, since the particles are first focused to the center of the flow channel and then pass into the measuring channel (both [0013] and [0016]). According to MPEP 2144.04 VI, C, a rearrangement of parts (such as focusing from upstream of the detector to on the detector) does not necessarily yield an unobvious invention. By example, "the particular placement of a contact in a conductivity measuring device was held to be an obvious matter of design choice. (In re Kuhle, 526 F.2d 553, 188 USPQ7 (CCPA 1975)" One of ordinary skill in the art would have known that moving the focusing step on to the detecting step would have yielded a simpler device, eliminating the need for extraneous microchannels between focusing and detection and possibly allowing for simpler electrode set-ups.

Concerning Claim 18, GAWAD teaches all the limitations of claim 14. Further, GAWAD teaches that the electrodes for sorting the cells after the measuring channel can be in pairs which are of different sizes (page 5, [0053]). It would have been *prima facie* obvious to one of ordinary skill in the art to use an array of electrodes of different sizes for focusing as well because of the greater control such an arrangement could afford the user while trying to focus particles, as is evidenced by the particle migration paths in figure 6d.

Concerning Claim 28, GAWAD teaches all the limitations of Claim 14. Further, GAWAD teaches that frequencies of 100kHz to 10MHz are used for the dielectrophoretic processes, such as focusing. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use a frequency filter to ensure that only these desired frequencies or those desired inside this range were used.

7. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over GAWAD in view of VADGAMA (US 6,300,123), from here on referred to as VADGAMA.

Concerning Claim 20, GAWAD teaches all the limitations of claim 19.

GAWAD does not expressly teach that the detector electrodes differ in shape in the direction parallel to fluid flow.

However, VADGAMA teaches an impedance measuring device in which the electrodes are of an interdigitated conformation (col. 3, lines 6-7). Such an electrode conformation would have two electrodes, each one comprised of a strip electrode with branching, forked finger electrodes spaced at regular intervals along the strip. These two would then be placed next to each other such that the spaces between each finger of one electrode were filled with a finger from the other electrode. Therefore the two electrodes would differ in shape along in the direction of flow, as they would be mirror images of each other.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use interdigitated electrodes in the device of GAWAD because

this electrode conformation has been shown to be effective in impedance measurements in intervening spaces between electrodes.

Concerning Claim 21, GAWAD in view of VADGAMA teaches all the limitations of claim 20. Further, GAWAD teaches at least one detector electrode (24 or 25 from figure 5a), which necessarily has an electrode structure. Examiner was unable to discern from common definition and the written description of "structure" how the claimed "electrode structure" necessarily differs over the prior art teaching of GAWAD.

Concerning Claim 22, GAWAD in view of VADGAMA teaches all the limitations of claim 21.

GAWAD does expressly teach that any electrode structure comprise an “electrode breakthrough”.

However, VADGAMA teaches an impedance measuring device in which the electrodes are of an interdigitated conformation (col. 3, lines 6-7). Such an electrode conformation would have two electrodes, each one comprised of a strip electrode with branching, forked finger electrodes spaced at regular intervals along the strip. These two placed next to each other such that the spaces between each finger of one electrode were filled with a finger from the other electrode. The spaces in between the fingers of interdigitated electrodes have been construed to read on the “electrode breakthrough”.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use interdigitated electrodes in the device of GAWAD because

this electrode conformation has been shown to be effective in impedance measurements in intervening spaces between electrodes.

Concerning Claim 23, GAWAD in view of VADGAMA teaches all the limitations of claim 21.

GAWAD does expressly teach that a partial electrode is integrated on the detector electrode.

However, VADGAMA teaches an impedance measuring device in which the electrodes are of an interdigitated conformation. Such an electrode conformation would have two electrodes, each one comprised of a strip electrode with branching, forked finger electrodes spaced at regular intervals along the strip. These two placed next to each other such that the spaces between each finger of one electrode were filled with a finger from the other electrode. The fingers of the interdigitated electrodes have been construed to read on "partial electrodes," as they are structural equivalents (each finger is integrated to the base strip electrode.)

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use interdigitated electrodes in the device of GAWAD because this electrode conformation has been shown to be effective in impedance measurements in intervening spaces between electrodes.

Concerning Claim 26, GAWAD teaches all the limitations of claim 25. Further, GAWAD teaches the presence of two offset electrodes which are arranged above and below the flow channel in the direction of fluid flow, such that one follows the other [0018].

GAWAD does not expressly teach that the electrodes be strips parallel to the direction of flow or have different widths or structured edges.

However, VADGAMA teaches an impedance measuring device in which the electrodes are of an interdigitated conformation. Such an electrode conformation would have two electrodes, each one comprised of a strip electrode with branching, forked finger electrodes spaced at regular intervals along the strip. These two would be placed next to each other or on top of each other such that the spaces between each finger of one electrode were filled with a finger from the other electrode. Necessarily, this also means that the electrodes are offset (as the regular features of each electrode alternate along the length of the coupled pairing). Additionally, the examiner has construed interdigitated electrodes to read on different structured edges because they are mirror images of each other and therefore have edges materially different from one another.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to substitute interdigitated electrodes for the electrodes of GAWAD because they have been proven effective in impedance measurement systems.

8. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over GAWAD in view of VADGAMA as applied to claims 20-23 and 25 above, and further in view of VEENSTRA et. al. (*Proteomics for biological discovery*, John Wiley and Sons, 2006), from here on referred to as VEENSTRA.

Concerning Claim 24, modified GAWAD teaches all the limitations of claim 23. Further, modified GAWAD teaches that the thickness of each electrode finger, which the

examiner has construed to be equivalent to the partial electrode, is 10 um thick (VADGAMA, col. 5, line 47).

Modified GAWAD does not expressly teach the size of the electrodes be equal to or less than the size of the particle's vertical projection (which is construed by the examiner to mean the cell's diameter.)

However, VEENSTRA teaches that the typical mammalian cell has a diameter of roughly 10 um (pg. 226, paragraph 4).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use interdigitated electrodes in the device of GAWAD because this electrode conformation has been shown to be effective in impedance measurements in intervening spaces between electrodes (VADGAMA, col. 3, lines 6-7). Further, the combination of these two inventions would have necessarily had electrodes of the claimed size, especially in light of VEENSTRA the applicant's disclosure which states the typical size of a biological cell to be between 2 and 20 um (page 14).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./
Examiner, Art Unit 1795

/Brian J. Sines/

Supervisory Patent Examiner, Art Unit 1795